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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

AUG 1 7 2005

AUGUET Michel, et al.

: Group: 1654

Serial No.: 09/937,306

Filed: 09/20/2001

For: COMBINATION.. ANTIOXIDANT

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August 17, 2005

## **RESPONSE**

Commissioner for Patents P.O. Box 1450 Alexandria, VA 22313-1450

Sir:

Responsive to the Office Action of June 2, 2005, Applicants request reconsideration of the application in view of the remarks presented herein.

The claims in the application are claims 1, 4 and 8 to 12, all other claims having been cancelled.

All the claims have been rejected under 35 U.S.C. 102 as being anticipated by the Naftchi et al. '933 (col. 133) or '962 (see col. 119). The Examiner has referred to No. 208 of '933. The Examiner was confused as to which example 1 Applicant was referring to which is directed to a different compound.

Applicants respectfully traverse this ground of rejection as the Naftchi et al. patents do not teach Applicants'invention which is directed to a mixture of a) NO syntahse inhibitory compound and b) a metabolic antioxidant compound possessing at least two thiol groups and which intervene in the Redox status of thiol groups. These are two separate compounds in admixture with each other. In contrast thereto, the compounds of Naftchi et al. patents are reaction products in both patents to form as compound 208 N-(1,2-dithionane-3-pentananido)-guanidine which is a single compound.

. . . . .

In the previous action, the Examiner took the position that Naftchi et al. start with lipoic acid and aminoguanidine and this teaches a mixture of the two compounds. Presumably, this is still the Examiner's position. However, this is an incorrect statement since lipoic acid and aminoguanidine are never admixed together. As can be seen from example 1 in column 8 of both patents, the carboxylic acid is never mixed with aminoguanidine but the acid is first mixed with thionyl chloride to form the acid chloride which is then reacted with guanidine hydrochloride. The same procedure was used in examples 2 to 14 in column 17 to form the compounds in Table II A in columns 9 to 16. In columns 97 and 98 of the Naftchi '962 patent, it is stated that compounds of Table II wherein compound 208 appears "are prepared according to the method described for preparing such compounds in accordance with this invention," which means by forming lipoic acid chloride which is then mixed with aminoguanidine and never is the acid physically admixed therewith. This means that the Examiner's assumption is incorrect and Naftchi et al. do not anticipate the invention nor render the same obvious.

All the claims have been rejected under 35 U.S.C. 103 as being obvious over the Naftchi et al., Petrus or Lai. The Examiner states that Lai teaches lipoic acid in line 62 of column 12 and aminoguanidine in lines 44-45 of column 21. With respect to Petrus, the Examiner refers to columns 3, 4, 7 and the claims without further comment.

Applicants respectfully traverse these grounds of rejection since Applicants' invention is not suggested by any of the references. The deficiencies of the Naftchi et al. patents is noted above and do not need to be repeated here. The Petrus patent is directed to a method of treating arthritis with a composition comprising an inhibitor of nitric oxide synthase and an amino sugar which is not an antioxidant. While aminoguanidine is cited in Claim 6 as a NOS inhibitor, there is no teaching in the reference of mixing an antioxidant with a NOS inhibitor without the presence of an amino sugar. If the Examiner is going to maintain this rejection, he is requested to indicate by line and column where in the reference that he finds such a teaching.

With respect to the Lai patent, there are listed 58 different classes of pharmacological agents which can be <u>conjugated</u> with nitric oxide scavengers through "<u>a covalent linkage</u>". There is no teaching of a mixture consisting of  $\alpha$ -lipoic acid and aminoguanidine. Therefore, none of the references renders obvious Applicants' mixture of NOS inhibitor with a metabolic antioxidant as defined in Applicants' claims and withdrawal of these rejections is requested.

In view of the above remarks, it is believed that the claims point out Applicants' patentable invention and favorable reconsideration of the application is requested.

\* \* \* \* \* \* \*

Respectfully submitted, Hedman and Costigan

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